

Centers for Medical Countermeasures against Radiation (CMCR) 2007 Annual Meeting Report

**Division of Allergy, Immunology and Transplantation (DAIT)
National Institute of Allergy and Infectious Diseases (NIAID)
National Institutes of Health (NIH)
Department of Health and Human Services (DHHS)**

June 18-19, 2007

CMCR Awardees

To expand the medical options available to triage, prevent and/or treat radiation-induced injury, NIH established eight Centers for Medical Countermeasures against Radiation (CMCRs) in September 2005. These Centers include Columbia University, Dana Farber Cancer Institute, Duke University, Fred Hutchinson Cancer Research Center, Medical College of Wisconsin, University of California, Los Angeles, University of Pittsburgh, and the University of Rochester.

Purpose of the Meeting

The primary objective was for the Centers to present research progress made during year two of the program funding. Other goals included fostering continued dialog and collaboration among the Centers, and facilitating interactions between the Centers and interested officials from the federal government. The meeting was held June 18-19, 2007 at the Holiday Inn on the Hill in Washington, DC. Presentations were grouped by topic into one of six sessions: Session I – Hematopoietic Injury, Session II – Gastrointestinal (GI) and Lung Injury, Session III – Biological and Physical Dosimetry, Session IV – Growth Factors & Antioxidants, Session V – Novel Mechanisms of Radiation Toxicity Modulation (Cytokines, Screening & Apoptosis) and Session VI – Training & Education/Pilot Projects Updates. The CMCR Principal Investigators (PIs) served as moderators, and all sessions ended with a discussion of the talks presented in each research area.

About the Meeting Attendees

Among the over 100 participants were CMCR PIs and their staff, NIAID representatives, and contractors receiving funding for product development support for radiation countermeasures. There were also representatives from the DoD, National Cancer Institute, Armed Forces Radiobiology Research Institute, Centers for Disease Control, Defense Advanced Research Projects Agency, Defense Threat Reduction Agency, Department of Energy, Food and Drug Administration, and the Office of Biomedical Advanced Research and Development Authority (BARDA). Please note: Because confidential, pre-publication data were presented at the meeting, only brief summaries of the presentations will be presented as part of this report.

Meeting Summary – Day One

The day commenced with a welcome from the NIAID program staff (given by Dr. Richard Hatchett), and continued with two presentations outlining evaluation of nuclear detonation effects on target populations (Mr. Brooke Buddemeier) and medical requirements that would be anticipated in the wake of a 10 kiloton nuclear detonation (Dr. Carl Curling). A discussion of different threat scenarios was then followed by a presentation from the BARDA (Dr. Joanna Prasher), which outlined their program for development and acquisition of medical countermeasure for radiological and nuclear threats.

Session I on hematopoietic injury began with a presentation from the Dana Farber Cancer Institute CMCR on mutant mouse models and their use in studying radiation-induced hematopoietic damage and repair. Attendees next heard about the advances in cell-based therapies being made at

the Fred Hutchinson Cancer Research Center including research on the possible use of: 1) myeloid progenitor cells, 2) umbilical cord blood, and 3) HLA-mismatched or HLA-haploidentical donors in hematopoietic cell transplants, and 4) use of enhanced supportive care for canine cell therapy models. Research being done within the Duke University CMCR on endothelial precursors as radiation protectants was presented, followed by the use of genetic modulation of bone marrow to reduce rejection (UCLA CMCR).

Beginning mid-day, Session II dealt with the study of the mechanisms involved in radiation-induced GI and lung damage and repair. Also discussed were potential countermeasures to mitigate and treat these forms of damage. Presentation topics included: potential agents for minimizing radiation-induced lung damage (Medical College of Wisconsin CMCR); two different studies being done at the University of Rochester CMCR on early molecular markers of progressive pulmonary damage, and the use of esculetin to protect and treat radiation-induced skin and lung injuries; and studies on the use of somatostatin analogs in the treatment of radiation-induced GI toxicity (Duke University CMCR).

Session III on Biological and Physical Dosimetry began with a presentation on the use of electron paramagnetic resonance (EPR) biodosimetry for triage of large groups of potentially-exposed individuals (University of Rochester CMCR). This was followed by a talk from the Columbia University CMCR on converting conventional biodosimetry assays from low- to high-throughput. Other research topics addressed during this session included the development of quantitative RT/PCR radiation dosimetry assays (Fred Hutchinson Cancer Research Center), and high-throughput radiation biodosimetry using gene expression profiles in a fully-integrated biochip (Columbia University CMCR).

In the final session of the day, testing of growth factors and anti-oxidants as potential mitigators and treatments of radiation injury was explored. This also included a discussion of mechanisms of radiation-induced oxidative stress. Specific talks focused on MnSOD nitration as a means of inactivation of radiation damage and oxidative lipidomics of the gamma irradiated intestine (both speakers from the University of Pittsburgh CMCR); cytokine therapy after total body irradiation (Fred Hutchinson CMCR); and radiation-induced chronic oxidative stress (Medical College of Wisconsin CMCR).

Meeting Summary – Day Two

Day two began with Session V, detailing advances by the Centers in identifying novel mechanisms of modulating radiation toxicity. Research updates were presented for the following topics: screening of new countermeasures and modification of radiation-induced carcinogenesis and cell death (UCLA CMCR), use of MnSOD gene therapy for radiation protection (University of Pittsburgh CMCR), and screening for activators of ATM signaling (Dana Farber Cancer Institute CMCR).

In the last public session (VI) of the meeting, Dr. Jacky Williams (University of Rochester CMCR) presented an update on the progress within the Education and Training Cores (common to all the Centers). In addition, three projects were selected by the CMCR PIs from among the pilots being funded at all the Centers to present their research findings. These presentations included talks on early biomarkers of radiation injury using the urine proteome (Medical College of Wisconsin), radiation exposure and erythropoiesis (University of Rochester), and GI toxicity in mouse models (MIT). The CMCR meeting then concluded with a closed business meeting in the afternoon for the CMCR steering committee.